# **Review Article:** Investigating the Effect of Hyaluronic Acid on Pain Control in Total Ankle Arthroplasty: A systematic review

# Vahid Fattahi<sup>1</sup>, Mohammad Irajian<sup>2®</sup>

<sup>1</sup> Assistant Professor, Department of anesthesiology, Faculty of medicine, Tabriz medical sciences, Islamic Azad University, Tabriz, Iran (Email: V\_Fattahi@gmail.com/ ORCID: 0000-0002-8231-7743)

<sup>2</sup>Assistant Professor of Orthopaedics, Department of Orthopedics, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran. (ORCID: 0000-0001-6599-2600)



**Citation** V. Fattahi, M. Irajian, **Investigating the Effect of Hyaluronic Acid on Pain Control in Total Ankle Arthroplasty: A systematic review**, *EJCMPR*. 2022; 1(5):23-40.

<sup>22</sup> <u>https://doi.org/ 10.5281/zenodo.8018260</u>

#### Article info:

Received: 01 December 2022 Accepted: 29 December 2022 Available Online: ID: EJCMPR-2306-1046 Checked for Plagiarism: Yes Peer Reviewers Approved by: Dr. Amir Samimi Editor who Approved Publication: Dr. Frank Rebout

Keywords: Arthroplasty, Pain, Hyaluronic Acid, Ankle Arthroplasty.

# ABSTRACT

The term arthroplasty refers to joint replacement through open surgery, which is used for cases where the joint has lost its function and the patient no longer has the ability to perform daily activities in the joint. In patients with knee osteoarthritis (arthrosis), the concentration of hyaluronic acid in the synovial fluid is lower than the normal value. As a result, by injecting hyaluronic acid (viscosupplementation), the patient's knee pain is reduced and the patient can carry out his daily activities as before. The pain reduction effect of hyaluronic acid injection usually lasts for 3 to 9 months, and after this period, the injection can be repeated up to 2 times. At this time, the surgeon can replace the joint by considering the patient's physical conditions as well as his age and activities. Joint replacement or arthroplasty is one of the methods considered to treat patients with advanced arthritis. Complications after arthroplasty are things that can be reduced by specialized physiotherapy. Many patients will gain appropriate abilities after surgery and recovery in physiotherapy clinics in such a way that they will return to normal conditions in daily activities, but some of them may need to extend the sessions or at least reduce the pain after surgery in different ways. The useful life of the joints depends on their conditions and how their use is different in different people and mainly the joints that bear more weight or those joints that are used more are more exposed to joint damage and destruction such as arthritis.

# Introduction

yaluronic acid is a naturally occurring substance in the human body. The highest amount of this substance is found in the fluids of the eyes (vitreous) and joints (joint fluid) [1]. The US Food and Drug Administration (FDA) has approved the use and injection of hyaluronic acid inside the knee for patients with knee arthritis. Hyaluronic acid is a humectant, a substance that retains moisture and can bind more than a thousand times its weight in water.

\*Corresponding Author: Mohammad Irajian (Mohammad\_irajian@yahoo.com)

#### 2022, Volume 1, Issue 5

#### Eurasian journal of Chemical, Medicinal and Petroleum Research

Hyaluronic acid, which is used medicinally, is either extracted from the cock's crown or made in the laboratory by a variety of bacteria. Also, injecting this substance into the eye is also used in patients with cataracts. The ankle is one of the sensitive joints of the body, which sometimes gets worn out and damaged due to heavy work, disease, bone abnormalities, etc [2-4]. There are different ways to treat these problems, including drug regimen, physical therapy exercises, and surgery. One of the surgery methods is called total ankle arthroplasty. The orthopedist uses this method only in the conditions of severe arthritis of the foot joint and not getting the desired result from non-surgical treatments. The ankle (tibiotalar) is one of the most important joints in the body, which consists of three bones: tibia, fibula, and talus. The tibia and fibula are related to the lower leg. The talus is also a small bone that is placed on the foot and is connected from above to the tibia and fibula and from below to the heel (Figure 1) [5].



Figure 1. Hyaluronic acid

These bones are firmly placed together by several ligaments and tendons (such as the Achilles tendon) and have created a joint capsule. The upper surface of the talus bone and the lower surface of the tibia are covered with cartilage. Cartilage layer is necessary for easy movement of bones together. Sometimes the function of the ankle joint is disturbed for various reasons. The reason for this can be the destruction and damage of the cartilage layer [6-8].

As a result, the movement of the bones together is difficult and causes pain, swelling and stiffness of the joint. Failure to treat these problems on time will result in severe pain and inability to move the ankle. Sometimes the severity of the symptoms is such that it prevents a person from doing daily activities. Of course, depending on the degree of damage, the mentioned symptoms are associated with severity and weakness.

When injecting hyaluronic acid in the knee, if there is swelling due to fluid accumulation in the knee joint, the excess joint fluid is aspirated before injection. In the first 48 hours after the injection, the patient should avoid putting pressure on his knee, such as standing for a long time, running or lifting heavy objects. Pain, warmth and slight swelling may be seen after injecting hyaluronic acid in the knee. Of course, these complications disappear after a short period of time. Cold compresses can be used to reduce these symptoms [9].

Hyaluronic acid is also used in cases such as joint disorders, urinary tract infections (UTI), stomach acid reflux, dry eyes, vaginal pain, skin aging and many other diseases. However, there is no acceptable scientific evidence to confirm the uses of this substance. Hyaluronic acid acts as a cushion or lubricant in joints and other tissues. In addition, it can also affect how the body reacts to injuries [10].

### What is the cause of ankle joint injury?

Destruction of the cartilage layer in the ankle joint occurs under the influence of various factors. The most important effective factors in this field are:

- Joint damage resulting from autoimmune diseases such as rheumatism, lupus, etc.;
- Abrasion resulting from heavy and continuous activities;
- Bone abnormalities in the ankle area;
- Decreased blood supply or tissue death (necrosis);
- Ankle fracture (trauma);
- Unsuccessful ankle surgery;
- Infection;
- Strike [11].

## How to diagnose an ankle injury?

People with ankle problems usually experience symptoms such as pain, stiffness, swelling and

reduced range of motion in this area. To diagnose the type of injury and its severity, the orthopedic specialist uses clinical examination and review of the patient's medical history. A more definitive diagnosis requires radiological imaging or MRI [12]. Sometimes, in addition to these cases, it is necessary to do a Doppler ultrasound. Because there is a possibility of ankle pain and swelling under the influence of a deep vein blood clot (vein wall thrombosis). There are different ways to treat problems caused by an ankle joint injury (Figure 2). Drug therapy, physiotherapy and surgery are among these. First, the orthopedist examines the patient's condition and tries non-invasive methods [13].

If the treatment with non-invasive methods is unsuccessful, surgery becomes necessary. Ankle joint surgery is performed in different ways. Among these cases, we can mention arthrosis (I dried up the joint) and arthroplasty. In arthroplasty, the ankle joint is partially or completely replaced with a prosthesis. The term ankle arthroplasty also refers to the same issue. Of course, this procedure is not only for ankles and is also used for other joints such as knees, hips, shoulders, elbows, etc. If the operation is performed correctly and adequate care is taken after it, problems such as pain, dryness and limited range of motion in the ankle will be reduced.





Figure 2. The effect of Application Hyaluronic acid at Arthroplasty

# The most important points before total ankle arthroplasty

Before the operation, it is necessary to observe the following points:

- Complete tests to ensure the patient's health (blood test, etc.);
- Inform the doctor about the history of the disease;
- Inform the doctor about the medications you are taking;
- Stopping the use of anticoagulants (such as aspirin) under the supervision of a doctor;
- Avoid eating and drinking for 8 hours before the operation;
- Having a companion for 1-2 weeks to help;
- Quit smoking a month before surgery;
- Stop drinking alcohol two weeks before the operation [14].

# How is total ankle arthroplasty performed?

To start the complete ankle arthroplasty operation, the patient is put under anesthesia or spinal anesthesia (from the waist down). Accessing the deep parts of the joint requires making an incision in front of the ankle. By removing the muscles, tendons and vessels of the joint capsule, it becomes visible. Then, separating the tibia and fibula from the talus bone is on the agenda. The damaged parts of the fibula and tibia are cut using a surgical saw. The purpose of this work is to create smooth surfaces for better attachment to the prosthesis [15].

Cutting the upper surface of the talus bone is also for the same purpose. The ankle prosthesis consists of three parts: Tibial interface plate, talus part and mobile support. The interface plate of the tibia and the talus piece are connected to the surfaces of the same name. The mobile support is also a plastic plate (made of polyethylene) that is placed between the two mentioned parts and facilitates their movement. Orthopedic specialist washes the area with saline solution after making sure the function of the implanted prosthesis is correct. Then the capsule is closed and sutured. The final stage includes the return of muscle, tendon, etc. to their place, skin suture and dressing.

# Types of complete ankle arthroplasty prosthesis

The artificial joint is divided into cemented and non-cemented types depending on how it is connected to the bone. In the type of cement, a special glue called cement connects the components together. In the non-cement type, the metal surfaces of the prosthesis are made of pores. Over time, bone grows into these holes and creates a strong connection [16].

# Postoperative care of total ankle arthroplasty

After the operation, the patient is admitted to the hospital for 1-2 days to monitor his condition closely. The pain resulting from the operation is also controlled using prescription drugs. The use of anti-analgesia device in the hospital is used to adjust the patient's pain medication. A splint or splint is also used to keep the wrist stable. It goes without saying that a tube is placed inside the ankle joint to prevent the accumulation of blood. This tube leads the extra blood out; it is removed 1-2 days after the operation. After complete ankle arthroplasty, it is necessary to do the following:

- Accurate and regular physical therapy exercises after the operation for 3 months to increase the range of motion of the ankle;
- Use a walker or cane for 6 weeks to prevent weight from being added to the ankle;
- Placing the ankle above the level of the heart to reduce pain and swelling;
- Avoiding exercise for one month after the operation;

- Using an ice pack to reduce swelling;
- Keeping the cut area dry and clean;
- Suture removal after 2 to 3 weeks (Figure 3) [17].

### **Complications of total ankle arthroplasty**

Total ankle arthroplasty, like other open surgeries, has various complications. Of course, today many improvements have been made in this field and its success rate has been increased. Complications are often caused by the low skill of the doctor or poor post-operative care. One of the side effects of this surgery is the risk of infection, which is seen in 2-4% of the treated people. Symptoms of infection include fever, inflammation, and discharge from the incision site. The source of infection can be a surgical site or an infection spread from other parts of the body. Although the infection is mild, it can be treated with antibiotics. But in severe cases, it is necessary to remove the ankle prosthesis. Another serious complication of total ankle arthroplasty is the loosening of the implanted prosthesis. Loosening is not unique to this joint and applies to all artificial joints with the difference that ankle sprains are more likely than others. Young people experience ankle sprains more often than the elderly. For this reason, the orthopedic specialist also considers the physical condition and age of the person before the surgery. Treatment of this problem requires re-surgery and prosthesis replacement. Other possible complications in this surgery include:

- Damage to the vessels and nerves of the ankle area during surgery, which causes anesthesia, etc.
- Thick skin scars (which sometimes require reconstructive surgery).
- Fracture of the tibia or fibula during surgery.
- Thrombosis or formation of clots in the lower blood vessels of the body.
- Sensitivity to the implanted joint.

- Limitation of movement in the ankle.
- Failure to relieve ankle pain.
- Joint dryness and weakness.

Sprained ankle.



Figure 3. Total ankle arthroplasty

# **Knee arthroplasty**

Athletes usually develop OCD or ankle cartilage damage in their knees, but because many people (not just athletes) ignore ankle sprains, ankle cartilage damage is also common. Since cartilage has very little ability to repair itself, if cartilage damage is not treated, it can progress to the stage of bone or joint erosion and lead to osteoarthritis. Cartilage damage is not limited to a specific age group. Injury is possible for all people, young and old, athletes or office workers (sitting behind a desk). A severe sprain in the ankle can lead to OCD [18-20]. When the injury is repeated or severe enough or neglected, the cartilage wears away and parts of it separate. This condition results in extremely painful boneon-bone contact.

# Symptoms of ankle cartilage damage

A person with an ankle cartilage injury will feel pain, swelling and stiffness in their ankle. This inflammation can be mild to severe. Also, the ankle can become red, hot, and extremely painful. The range of motion of the ankle can also be limited, in which case the person will not be able to move the ankle easily [21].

# **Causes of ankle cartilage pain**

If the cartilage is damaged or worn away, the joint becomes painful and stiff and has a reduced range of motion. In severe osteoarthritis, the hyaline cartilage can be completely destroyed, leaving the affected joint without regeneration. This causes the bones to rub against each other. Osteophytes may also develop due to excess stress on the ends of the bones at the joint margin. This results in significant pain, loss of motion, and poor performance.

### Eurasian journal of Chemical, Medicinal and Petroleum Research

# The importance of cartilage

Cartilage is a white, connective tissue found in joints and many parts of the body. For example, the nose and ears are relatively and completely composed of cartilage. Cartilage acts as a cushion-like material between the joints and supports the bones against wear and tear. Cartilage also holds bones together. Cartilage is not a bone but a hard and flexible tissue that is easily damaged. No blood flow goes to the cartilage and that is the reason why it is white. Cartilage does not heal easily when it is damaged or torn due to lack of blood flow.

# What is the function of ankle cartilage?

Ankle arthroscopy is a minimally invasive surgery that diagnoses or treats many ankle problems. Common problems include infection, injury, arthritis, inflammatory conditions, and undiagnosed ankle symptoms. In ankle arthroscopy, an arthroscopic with a small camera is used to view the inside of the ankle joint. Special instruments allow your doctor to treat joint problems through small incisions. Ankle arthroscopy can relieve symptoms and restore range of motion. Ankle arthroscopy is a common surgery, but it involves some risks and potential complications. Consider all your treatment options before undergoing ankle arthroscopy [22].

# Other surgical procedures that may be performed

Your doctor may also do a biopsy. A biopsy involves removing a sample of cells or tissue and testing it for cancer and other diseases. You may need open surgery (ankle arthrotome) for an ankle condition that your doctor cannot treat with arthroscopy. Open surgery involves making a longer incision that allows you to see and treat the ankle directly.

### Why is ankle arthroscopy performed?

A doctor may recommend an ankle arthroscopy to diagnose ankle symptoms if the cause is unknown. Ankle arthroscopy is not the first choice for treating ankle diseases. Your doctor may recommend ankle arthroscopy to diagnose or treat:

- Infection of the ankle joint, also called septic arthritis.
- Ankle joint injuries, including fractures, ligament tears, cartilage tears, and overuse injuries.
- Inflammatory forms of arthritis, including rheumatoid arthritis.
- Loose bodies, including bone fragments and cartilage fragments.
- Arthritis or degenerative joint disease, which is the breakdown of cartilage and bone.
- Synovitis, or inflammation of the inner lining of a joint.
- Unknown ankle symptoms including: pain, swelling, locking, cramping and...

# Who performs ankle arthroscopy?

Orthopedic surgeons and foot and ankle surgeons perform ankle arthroscopy. Orthopedic surgeons are specially trained to treat problems of the bones and joints [23].

# Cause of ankle cartilage damage Abnormal ankle alignment (deviation)

Sometimes this is congenital and sometimes it is caused by healing after an injury. This condition must be corrected by surgery and therapy.

#### **Damage and overuse**

Falling on the stairs, twisting the ankle, dropping an object and falling on the ankle, all of these can cause damage to the ankle cartilage. As you may know, athletes in football, rugby, tennis and wrestling are most likely to suffer from this condition. Any sports such as basketball or badminton that involve high contact or running and jumping are also excluded.

## Lack of mobility

Muscle atrophy (weakening) isn't the only thing that happens when a person is inactive. Joints need mobility to stay healthy. Long periods of inactivity and lack of activity may also damage the ankle cartilage.

### **Obesity**

Our body is great at adapting and adjusting itself, but excess weight causes many sprains in body parts, including bones and joints (especially the ankle area). Ankle joints are the joints that support the weight of the body and every time a person walks, these joints support him. Obese people's bodies are under more physical stress, which is why they are more likely to develop cartilage damage in their ankles [24].

**Complications of ankle cartilage damage** Cartilage damage can lead to:

## Hem arthrosis or bleeding in the joint

In severe cases, a piece of cartilage separates and gets stuck between the joints. This condition causes joint locking and bleeding. Also, in this case the ankle looks bruised.

### Extra pressure on the bones

Extra pressure on the bones can also lead to bone spurs or osteophytes. These bone spurs are formed on the edge of the joint and cause more severe pain and more disturbance in ankle function. This situation is like gears that are pressed against each other but do not move and they make noise from the place where they scratch each other.

# Ankle cartilage damage

In this case, a cavity is created in the cartilage. This cavity, like all cavities, can become larger and reach the point where the entire cartilage is lost. When the cartilage is completely destroyed, the joints lose their cushion-like components and the bones rub against each other, which is very painful. Ankle joints are weight-bearing joints, and if their cartilage is damaged, the patient will lose the ability to walk. Joints need mobility to stay healthy. Long periods of immobility and lack of activity also damage the cartilage [25].

## **Diagnosis of cartilage damage**

Distinguishing cartilage damage from other problems (such as ligament damage or subchondral bone lesions) can be difficult because they all have similar symptoms. To confirm cartilage damage, the person is examined by a specialist with a simple X-ray. If the answer is negative and the pain continues for more than 2 months, CT scan and MRI imaging are performed. MRI and CT scan show cartilage damage, sub-cartilage bone damage or fracture of a piece of bone or cartilage, which is also very painful. Also, a person with this condition produces a clicking sound whenever he moves his ankle (Figure 4).



Figure 4. Diagnosis of cartilage damage

# Treatment of ankle cartilage pain

As with other ankle problems, there are several treatment options for OCD, including:

# Non-steroidal anti-inflammatory drugs

The doctor prescribes non-steroidal antiinflammatory drugs to reduce pain and inflammation.

# **Physiotherapy**

The person is usually referred to a physical therapist to strengthen their muscles, regain joint range of motion, and increase their sense of balance [26].

# Resting the ankle and doing alternative movements

In order to minimize the pain, a person should avoid activities that cause ankle pain. For example, instead of taking the stairs, you can choose to ride a bicycle instead of walking.

## joints (splint or brace)

Ankle braces are plastic or leather pieces that protect the ankle joints and significantly reduce pain in that area.

# Ice

In severe cases, a person can apply an ice compress on his ankle 3 to 4 times a day for 20 minutes. This should be done immediately after physical activity.

# Surgery

When treatments and medications are not enough to help relieve pain and improve mobility, ankle surgery may be needed. With ankle arthroscopy, cartilage pieces can be removed and the bed of the lesion can be pierced so that the stem cells penetrate from the bottom of the lesion and cause repair. Open ankle surgery can also be a solution. For cases where the damage is more severe and the size of the large, cartilage grafting may be the only solution [27-29].

# **Cartilaginous ankle drug**

Today, supplements called glucosamine or socalled (cartilaginous drugs) have entered the market, and these supplements are capable of building cartilage or repairing cartilage. People use glucosamine sulfate orally to treat a painful disease caused by inflammation, breakdown and destruction of cartilage (arthrosis). Glucosamine is a natural compound found in cartilage, the tough tissue that strengthens joints.

# Uses of glucosamine for

- Arthritis: Oral glucosamine sulfate may reduce pain for people with knee arthritis. Some research suggests that it may help slow down the rate of knee joint destruction associated with osteoarthritis. Another benefit of glucosamine sulfate supplement is for hip, spine, hand or ankle arthritis.
- Rheumatoid arthritis: Early research suggests that oral glucosamine hydrochloride may reduce pain associated with rheumatoid arthritis. However, the researchers did not see an improvement in inflammation or the number of painful or swollen joints [30].

# Arthroscopy aimed at repairing OCD in orthopedics

Unfortunately, without surgery, OCD will get worse and worse. It is not desirable for this problem to progress to the point where a complete replacement of the joint is required. Arthroscopy can repair cartilage damage and a person can return to their previous quality of life and daily activities as quickly as possible through rest and treatment.

#### 2022, Volume 1, Issue 5

# After arthroscopic surgery

In order to relieve pain and inflammation, the person is given oral painkillers for several days. Sutures are removed 1 to 2 weeks after surgery. At this stage, the treating doctor provides recommendations regarding range of motion, ankle exercises and physical therapy to his patients, which are ideal for them. Depending on the patient's condition, he may be able to walk on his feet again immediately after surgery, or he may be able to keep them elevated and non-weight bearing for several weeks [31-33].

# Arthroscopy recovery period of ankle cartilage

70 to 90 percent of patients who have undergone arthroscopic surgery for the treatment of ankle cartilage lesion (OCD) have obtained excellent results. A person can expect to return to work a few days after surgery. Of course, this is if there is no pressure on his legs. Most patients need 1-2 weeks to recover. It is best to ask your doctor about your condition. A person can drive again when they are able to put weight on their legs and stop taking narcotic pain medications. If a person is an athlete or is very interested in exercising, he should wait at least 4 to 6 months and sometimes up to a year to return to his favorite sport. This period should also be accompanied by physiotherapy [34].

## Orthopedic surgery in the corona era

Corona or Covid-19 is an unknown virus that has affected most countries in the world these days. This virus has a very high transmission speed, which is the reason for its rapid spread. The emergence of Covid-19, in addition to the severe economic decline worldwide, has created many other problems, especially for patients who need surgery. Patients who need surgery for any reason, such as knee joint replacement, treatment of meniscus tears, treatment of cruciate ligament ruptures, as well as lumbar disc and cervical disc, in the days when we are dealing with corona disease, it is preferable to perform the surgeries a little later until the spread of Corona is less.

# Treatment of disc patients in the corona era

Patients who have severe neck and back pain or have acute disc herniation, our advice is to see a doctor. We can try to help them by using the more powerful treatments we have available. In cases where the lumbar disc or neck disc is very severe, intra spinal injections can also be used. There are many patients whose discs are very severe and need surgery, but it is possible to treat the patients' discs using spinal injections.

# Treatment of meniscus and cruciate ligament tear patients in the Corona era

For patients with torn meniscus and cruciate ligament, if they are not in severe pain and their knee is not locked, intra-articular injections can be used for their recovery, but if their problem is acute and they need surgery. By using intraarticular injections, their pain and inflammation can be reduced so that they can undergo arthroscopic surgery at the right time after the end of the Corona period [35].

Is orthopedic surgery possible during the corona outbreak? Patients who suffer from back disc pain, severe arthritis, meniscus tear, and knee cruciate ligament tear in a very acute form, if they really need surgery, there are currently centers that are now called white centers. We can perform surgery for these patients with health protection and tests that are taken from the patient before the operation, and there will be no problems. All patients who enter this hospital are first subjected to a CT scan of the lungs, necessary tests for the diagnosis of corona and blood tests. If the patient's corona test is negative, we will admit them and perform surgery. Therefore, according to the amount of damage and the needs of the patients, it can be decided for them whether they need surgery or not [36].

# Carpal tunnel syndrome surgery in the Corona era

Patients who need minor surgeries, such as carpal tunnel syndrome, should see their orthopedic doctor. Currently, there are effective drug treatments for this category of patients that can be used. Be sure to use a wristband to reduce their pain and discomfort. Surgery can be performed for these patients in the next one to two weeks. Of course, before the operation, a CT scan of the lungs and Corona-related tests should be taken from the patient.

# Non-union of the fracture

Chronic Nonunion with modern treatment methods, most broken bones heal without any problems. After the treatment of the broken bone, new bone tissue begins to form and the broken pieces are connected to each other. Some broken bones do not heal even when they receive the best surgical or non-surgical treatment. In some cases, certain risk factors make bone healing less likely, and in some cases, healing takes longer than usual.

### **Bone healing**

For bone healing to occur, the bone needs sufficient stability (to be in a fixed place) and blood supply. Proper nutrition also plays a role in bone repair.

- Blood supply. Blood brings components needed for repair to the fracture site. These include oxygen, healing cells, and chemicals necessary for healing (growth factors). Blood supply to the damaged bone usually returns on its own during the healing period.
- Stability. All treatments for broken bones follow one basic rule: The broken pieces must be reattached and immobilized until they heal. Some fractures can be held in place with plaster. Some fractures require surgical fixation with devices such as

screws, plates, rods, and frames. A fractured bone is fixed with a plate and screw.

> Nutrition. A broken bone also needs adequate nutrition to heal. The best way to ensure proper nutrition is to eat a healthy, balanced diet that includes protein, calcium, vitamin C, and vitamin D. Dietary supplements that exceed the daily requirement are not effective. (Except for some. rare patients with severe malnutrition with many organs affected. In this case, the doctor will discuss the dietary guidelines and provide recommendations for adding nutritional supplements.) [37].

### **Causes of fracture non-union**

Nonunion occurs when the bone lacks sufficient stability, blood flow, or both. Also, if the bone is broken due to a major injury such as a car accident, it is more likely to suffer from chronic non-union because severe injuries often disrupt the blood supply to the broken bone (Figure 5).

# **Risk factors**

Several factors increase the risk of bone nonunion.

- The use of tobacco or nicotine in any form (smoking, chewing tobacco and using gum or nicotine patches) causes the bone not to repair and increases the chance of non-union;
- Old age;
- Severe anemia;
- Diabetes;
- Vitamin D levels are low;
- Hypothyroidism;
- Inappropriate feeding;
- Infection;
- A severe fracture that has an open wound;
- Anti-inflammatory drugs such as aspirin, ibuprofen and prednisone. The doctor and the patient should always

discuss the risks and benefits of using these drugs during fracture repair.

## **Blood supply**

If the damaged bone does not have good and sufficient blood supply, it is more likely that it will not heal. Some bones, such as the leg bones, have inherent stability and excellent blood supply. They can be expected to improve with minimal treatment time. Some bones, such as the upper femur (femoral head and neck) and the small wrist bone (scaphoid), have limited blood supply. When these bones are broken, the blood supply is cut off. Some bones, such as the lower leg (tibia), have a moderate blood supply. However, injury can disrupt it. For example, a severe injury can damage the skin and muscles over the bone and cut off the external blood supply. In addition, the damage can destroy the internal blood supply in the brain in the center of the bone [38].









## Symptoms of fracture non-union

Patients with chronic fractures usually feel pain at the fracture site for a long time after the initial pain of the fracture has disappeared. This pain may last for months or even years. The pain may be constant and always present, or it may occur only when using the broken arm or leg.

# **Doctor's examination**

To diagnose chronic nonunion, the doctor uses imaging studies that provide detailed images of the bone and surrounding soft tissue. Depending on the bone involved, these tests may include Xrays, computed tomography (CT) scans, and magnetic resonance imaging (MRI). Imaging studies allow the doctor to see the broken bone and track its healing process.

# Chronic nonunion may be diagnosed if a doctor finds one or more of the following

If diagnosed, the doctor may order a blood test to investigate the cause. These tests may reveal an infection or other medical condition, such as anemia or diabetes, that may slow the bone healing process.

- Persistent pain at the fracture site;
- Continuous fissure at the fracture site without bone growth;

- No improvement in bone healing over several months compared to repeated imaging studies;
- Inadequate treatment within a period of time usually sufficient for normal recovery.

# **Treatment of fracture nonunion**

Non-surgical and surgical treatments for chronic fractures have advantages and disadvantages. More than one treatment may be appropriate. Talk to your doctor about the unique benefits and risks of your treatment. Your doctor will recommend the right treatment option for you.

# **Non-surgical treatment**

Some chronic fractures can be treated without surgery. The most common non-surgical treatment is bone stimulation. A small device sends out ultrasonic waves or electromagnetic pulses that heal the patient. The patient puts the stimulator on the skin where the fracture is for 20 minutes to several hours every day. This treatment must be used every day to be effective. An external bone stimulator is applied to the skin over the fracture site [39].

### **Surgical treatment**

Surgery is needed when non-surgical methods fail. If the first surgery fails, you may need a second surgery. Surgical options include bone graft or bone graft substitute, internal fixation, and/or external fixation.

Bone grafting. During this procedure, the bone from another part of the body begins the healing process at the fracture site. A bone graft provides a scaffold upon which new bone may grow. Bone grafting also provides new bone cells and the body's natural chemicals for bone repair. During the operation, the surgeon makes an incision and removes pieces of bone from different areas of the patient. Then they are transplanted to the fracture site. The edge of the pelvis or "Iliac crest" is mostly used to

remove the bone. Although bone removal may be painful, the amount of bone removed usually does not cause functional, structural, or cosmetic problems. A bone graft is taken from the back of the pelvis and placed at the fracture site.

- Allograft (bone graft from another person). Allograft bone grafting avoids removing bone from the patient. Bone or tissue grafts are transplanted from one person to another, thus reducing the pain caused by the treatment. Like bone grafting in old methods, a scaffold is provided to heal the patient's bone in the fracture area. Over time, the patient's bone replaces the allograft bone. Although there is a risk of infection, allograft bone grafts are processed and sterilized to minimize this risk.
- **≻**Bone graft substitutes and/or osteobiologics. Like allografts, bone graft substitutes prevent bone removal and pain. Although bone graft substitutes do not provide the new bone cells needed for normal repair, they do provide the scaffolding chemicals needed for growth. Depending on the type of fracture, any of the above materials or a combination of them may be used to fix the fracture. Bone grafting (or bone graft substitutes) alone does not provide any stability to the fracture site. Unless the fracture is inherently stable, you may need additional surgical procedures (internal or external fixation) to improve stability.
- Internal fixation. Internal fixation stabilizes the fracture. The surgeon attaches metal plates and screws to the outer part of the bone or inserts a nail (rod) into the inner canal of the bone. If a fracture develops after internal fixation surgery, another internal fixation surgery may be needed to increase stability. The surgeon may use a stronger device such as a larger rod (nail) or a longer plate. Removing the previously inserted nail and placing a larger rod (replacement rods) increases

stability and stimulates healing within the bone. Internal fixation can be combined with bone grafting to help stabilize and stimulate healing.

**External fixation.** External fixation also stabilizes the damaged bone. The surgeon attaches a rigid frame to the outside of the affected arm or leg. The frame is attached to the bone with wires or pins. If instability has contributed to a chronic fracture, external fixation may be used to increase stability of the fracture site. External fixation can treat a chronic fracture. External fixation is effective in treating chronic fractures in patients with infection or in patients who have lost bone. An external fixator made of screws and wires stabilizes the tibial fracture [40]. To determine the cause of broken bones not healing, scientists are investigating natural chemicals that the body needs to repair bones. These chemicals are called growth factors. When a bone breaks, it is normally produced in the body in a certain order. Other chemicals can reduce the likelihood of bone healing. Researchers are focused on synthesizing these chemicals and determining the ideal way to prevent negative factors or increase positive factors for damaged bone. One day, doctors may be able to inject chemicals directly into nonunion to induce healing. If none of the control measures, drugs and treatment methods work, the orthopedic specialist recommends joint replacement surgery or arthroplasty [41]. Using this operation, the damaged joint is removed and replaced, and as a result, the person's movement problems are improved and the pains caused by joint destruction are also eliminated [42].

# Conclusion

In a simple definition, it can be said that arthroplasty is a treatment method that replaces the damaged joint with an artificial joint, such as knee replacement. You may know that the thigh joint, also known as the hip joint, is one of the most mobile joints in the human body and plays a very important role in walking and maintaining balance. This joint is located on both sides of the hip joint and connects the upper body to the lower limbs. The damaged parts of the pelvis are removed and replaced with artificial parts made of metal and hard plastic. An artificial joint (prosthesis) should help reduce pain and improve hip function. The rate of complications after joint replacement surgery is very low. Serious complications such as joint infection occur in less than 2% of patients. However, as with any major surgical procedure, patients undergoing total joint replacement are at risk of certain complications, many of which can be successfully avoided and/or treated.

# **Blood clotting**

This is the most common complication after surgery. Your orthopedic surgeon may prescribe one or more measures to prevent clots from forming in the veins of your leg veins. These measures may include a special support hose, inflatable leg covers, and blood thinners.

### Fracture

Healthy parts of the pelvis may be broken during surgery. Smaller fractures should heal on their own, but larger fractures may require the use of wires, pins, and possibly bone grafts for repair.

## **Dislocation**

Because certain positions may cause the ball of your new joint to shift, it is recommended not to bend more than 90 degrees at the hip and not allow your legs to cross the midline of your body. If a dislocation occurs, a secondary surgery may be required to stabilize it. Change in leg length: Although the surgeon will do his best to prevent this, sometimes muscle weakness around the thigh can cause the leg to shorten or lengthen with the new thigh.

#### Loosen

This is rare, but if the new joint doesn't settle on your bone over time or loosens over time, surgery may be needed to fix the problem.

# **Replacement of the second hip joint**

Depending on your age and activity level, your new hip replacement may wear out over time. If this is the case, it is likely that a second hip replacement will be performed, although the new materials will make the artificial hip last longer.

### References

[1]Abdollahi MH, Foruzan-Nia K, Behjati M, Bagheri B, Khanbabayi-Gol M, Dareshiri S and et al. The effect of preoperative intravenous paracetamol administration on postoperative fever in pediatrics cardiac surgery. Nigerian medical journal: journal of the Nigeria Medical Association. **2014**; 55(5): 379. [Google Scholar], [Publisher]

[2]Birmangi S, A Review of the Effect of Corona on the Human Brain – Short Review, Eurasian Journal of Chemical, Medicinal and Petroleum Research, **2022**, 1 (3), 80-87 [Crossref], [Google Scholar], [Publisher]

[3]Ebadian B, Fathi A, Khodadad S. Comparison of the effect of four different abutment screw torques on screw loosening in single implantsupported prosthesis after the application of mechanical loading. International Journal of Dentistry. **2021**;19;2021: 3595064.[Google Scholar], [Publisher]

[4]Eghdam-Zamiri R, Gol MK. Effects of ginger capsule on treatment of nausea and vomiting in patients receiving cisplatin undergoing mastectomy: a randomized clinical trial. The Iranian Journal of Obstetrics, Gynecology and Infertility. **2020**;22(11): 15-21. [Crossref], [Google Scholar], [Publisher]

[5]Elmi A, Rouhani A, Irajian M, Iman MB, Tabrizi A. Comparison results of acromioclavicular dislocation treatment by screw with and without coracoclavicular ligamentous repair. Medical Journal of Tabriz University of Medical Sciences. **2017**; 39(2): 46-51. [Google Scholar], [Publisher]

[6]Esmaeilzadeh AA, et al., Correction: Recent advances on the electrochemical and optical biosensing strategies for monitoring microRNA-21: a review, Analytical Methods, **2023** [Crossref], [Google Scholar], [Publisher]

[7]Esmaeilzadeh AA, et al., Cytotoxic study of green synthesized pure and Ag-doped  $\alpha$ -Fe2O3 nanoparticles on breast cancer (MCF-7) cell line, Nanomedicine Research Journal, **2022** 7 (4), 370-377 [Crossref], [Google Scholar], [Publisher]

[8]Esmaeilzadeh AA, et al., Recent advances on electrochemical and optical biosensing strategies for monitoring of microRNA-21: A review, Analytical Methods, **2022** 15 (1), 132-132 [Crossref], [Google Scholar], [Publisher]

[9]Esmaeilzadeh AA, et al., Study of Silybin in Plant Effective Substance for use in targeted liposomal nanoparticles in the treatment of liver cancer, Archives of Pharmacy Practice, **2020** 11 (1), 35 [Google Scholar], [Publisher]

[10] Esmaeilzadeh, AA, et al., Identify Biomarkers and Design Effective Multi-Target Drugs in Ovarian Cancer: Hit Network-Target Sets Model Optimizing, Biology, **2022**, 11 (12), 1851 [Crossref], [Google Scholar], [Publisher]

[11] Gheisari R, Doroodizadeh T, Estakhri F, Tadbir A, Soufdoost R, Mosaddad S. Association between blood groups and odontogenic lesions: a preliminary report. Journal of Stomatology. **2019**;72(6):269-73. [Crossref], [Google Scholar], [Publisher]

[12] Gheisari R, Resalati F, Mahmoudi S, Golkari A, Mosaddad SA. Do Different Modes of Delivering Postoperative Instructions to Patients Help Reduce the Side Effects of Tooth Extraction? A Randomized Clinical Trial. Journal of Oral and Maxillofacial Surgery. **2018**;76(8):1652.e1-.e7.[Crossref], [Google Scholar], [Publisher]

[13] Haghdoost M, Mousavi S, Gol MK, Montazer M. Frequency of Chlamydia

### 2022, Volume 1, Issue 5

trachomatis Infection in Spontaneous Abortion of Infertile Women During First Pregnancy Referred to Tabriz University of Medical Sciences by Nested PCR Method in 2015. International Journal of Women's Health and Reproduction Sciences. **2019**; 7(4): 526-30. [Google Scholar], [Publisher]

[14] Hasanpour Dehkordi A, Khaji L, Sakhaei Shahreza MH, Mashak Z, Safarpoor Dehkordi F, Safaee Y, Hosseinzadeh A, Alavi I, Ghasemi E, Rabiei-Faradonbeh M. One-year prevalence of antimicrobial susceptibility pattern of methicillin-resistant Staphylococcus aureus recovered from raw meat. Tropical Biomedicine. **2017**;34(2):396-404. [Crossref], [Google Scholar], [Publisher]

[15] Irajian M, Beheshtirooy A. Assessment of Frequency of Long Bone Osteomyelitis in Traumatic Patients Undergoing Orthopedic Surgery in Imam Reza (AS) Hospital-Tabriz. International Journal of Current Microbiology and Applied Sciences. **2016**;5(1): 818-825.[Google Scholar], [Publisher]

[16] Irajian M, Faridaalaee G. Establishing a field hospital; a report on a disaster maneuver.
Iranian Journal of Emergency Medicine. **2016**;3(3): 115-118. [Crossref], [Google Scholar], [Publisher]

[17] Khaji L, Shahreza MH. SCCmec types in methicillin-resistant Staphylococcus aureus strains of various types of milk. Electronic Journal of Biology. **2016**;13:1. [Google Scholar], [Publisher]

[18] Mahmoodpoor A, Hamishehkar H, Fattahi V, Sanaie S, Arora P, Nader ND. Urinary versus plasma neutrophil gelatinase-associated lipocalin (NGAL) as a predictor of mortality for acute kidney injury in intensive care unit patients. Journal of Clinical Anesthesia.**2018**; 14: 12-17.[Crossref], [Google Scholar], [Publisher]

[19] Mahmoodpoor A, Hamishehkar H, Shadvar K, Sanaie S, Iranpour A, Fattahi V. Validity of bedside blood glucose measurement in critically ill patients with intensive insulin therapy. Indian Journal of Critical Care Medicine.**2016**; 20(11): 653. [Crossref], [Google Scholar], [Publisher]

[20] Margy S, A Review of the Effect of Brain imaging- Short Review, Eurasian Journal of Chemical, Medicinal and Petroleum Research, **2022**, 1 (3), 88-99 [Google Scholar], [Publisher] [21] Mashak Z, Jafariaskari S, Alavi I, Sakhaei Shahreza M, Safarpoor Dehkordi F. Phenotypic genotypic assessment of antibiotic and resistance and genotyping of vacA, cagA, iceA, oipA, cagE, and babA2 alleles of Helicobacter pylori bacteria isolated from raw meat. Infection Resistance. 2020 29:257-72. and Drug [Crossref], [Google Scholar], [Publisher]

[22] Mobaraki-Asl N, Ghavami Z, Gol MK. Development and validation of a cultural competence questionnaire for health promotion of Iranian midwives. Journal of education and health promotion. **2019**;8:179. [Crossref], [Google Scholar], [Publisher]

[23] Mokhtari Ardekani AB, et al., miR-122 dysregulation is associated with type 2 diabetes mellitus-induced dyslipidemia and hyperglycemia independently of its rs17669 variant, BioMed Research International, **2022**, Article ID 5744008, [Crossref], [Google Scholar], [Publisher]

[24] Mosharraf R, Molaei P, Fathi A, Isler S. Investigating the Effect of Nonrigid Connectors on the Success of Tooth-and-Implant-Supported Fixed Partial Prostheses in Maxillary Anterior Region: A Finite Element Analysis (FEA). International Journal of Dentistry. **2021**; 12;2021: 5977994.[Crossref], [Google Scholar], [Publisher]

[25] Movassagi R, Montazer M, Mahmoodpoor A, Fattahi V, Iranpour A, Sanaie S. Comparison of pressure vs. volume-controlled ventilation on oxygenation parameters of obese patients undergoing laparoscopic cholecystectomy. Pakistan journal of medical sciences.**2017**; 33(5): 1117 .[Crossref], [Google Scholar], [Publisher]

[26] Nazari B, Amani L, Ghaderi L, Gol MK. Effects of probiotics on prevalence of ventilatorassociated pneumonia in multitrauma patients hospitalized in neurosurgical intensive care unit: a randomized clinical trial. Trauma Monthly.**2020**; 25(6): 262-268. [Crossref], [Google Scholar], [Publisher]

[27] Ranjbar R, Safarpoor Dehkordi F, Sakhaei Shahreza MH, Rahimi E. Prevalence, identification of virulence factors, O-serogroups and antibiotic resistance properties of Shigatoxin producing Escherichia coli strains isolated from raw milk and traditional dairy products. Antimicrobial Resistance & Infection Control. **2018**;7(1):1-1. [Crossref], [Google Scholar], [Publisher]

[28] Ranjbar R, Shahreza MH, Rahimi E, Jonaidi-Jafari N. Methicillin-resistant Staphylococcus aureus isolates from Iranian restaurant food samples: Panton-Valentine Leukocidin, SCCmec phenotypes and antimicrobial resistance. Tropical Journal of Pharmaceutical Research. **2017** 7;16(8):1939-49. [Crossref], [Google Scholar], [Publisher]

[29] Ranjbar R, Shahreza MH. Prevalence, antibiotic-resistance properties and enterotoxin gene profile of Bacillus cereus strains isolated from milk-based baby foods. Tropical Journal of Pharmaceutical Research. **2017** 7;16(8):1931-7. [Crossref], [Google Scholar], [Publisher]

[30] Saliminasab M, Jabbari H, Farahmand H, Asadi M, Soleimani M, Fathi A. Study of antibacterial performance of synthesized silver nanoparticles on Streptococcus mutans bacteria. Nanomedicine Research Journal. **2022** 1; 7(4): 391-6.[Google Scholar], [Publisher]

[31] Sarejloo SH, et al., Neutrophil-to-Lymphocyte Ratio and Early Neurological Deterioration in Stroke Patients: A Systematic Review and Meta-Analysis, **2022**, Article ID 8656864 [Crossref], [Google Scholar], [Publisher] [32] Shahreza MH, Rahimi E, Momtaz H. Shigatoxigenic Escherichia coli in ready-to-eat food staffs: Prevalence and distribution of putative virulence factors. Microbiology Research. **2017** 22;8(2):7244. [Crossref], [Google Scholar], [Publisher]

[33] Shahreza MS, Dehkordi NG, Nassar MF, Al-Saedi RM. Genotyping of Campylobacter jejuni isolates from raw meat of animal species. Academic Journal of Health Sciences: Medicina balear. 2022;47(4):52-7. [Crossref], [Google Scholar], [Publisher]

[34] Shahreza MS, Dehkordi NG, Nassar MF, Al-Saedi RM. Virulence characters and linotyping of Pseudomonas aeruginosa isolated from meat and assessment of the antimicrobial effects of Zataria multiflora against isolates. Academic Journal of Health Sciencies: Medicina Balear. **2022**. 37(4): 11-16. [Google Scholar], [Publisher]

[35] Shahreza MS. Ready To Eat Food Samples As Reservoirs Of Shiga Toxigenic Escherichia Coli. Journal of Pharmaceutical Negative Results. 2022 31:9761-6. [Crossref], [Google Scholar], [Publisher]

[36] Shahreza, M. H. S., & Soltani, A. Genotyping and antibiotic resistance of methicillin-resistant staphylococcus aureus strains isolated from raw and frozen meat samples and assessment of the antimicrobial effects of origanum vulgare against MRSA isolates. International Journal of Health Sciences, **2022**, 6(S6), 4840–4852. [Google Scholar], [Publisher]

[37] Shahreza, M. S., & Afshari, H. Ribotyping and assessment of toxigenic genes of clostridium difficile strains isolated from raw meat. International Journal of Health Sciences, **2022**, 6(S6), 4853–4863. [Crossref], [Google Scholar], [Publisher]

[38] Tahmasebi E, Alam M, Yazdanian M, Tebyanian H, Yazdanian A, Seifalian A, et al. Current biocompatible materials in oral regeneration: a comprehensive overview of composite materials. Journal of Materials

Eurasian journal of Chemical, Medicinal and Petroleum Research

Research and Technology. 2020;9(5):11731-55. [41] Yahaghi E, Khamesipour F, Mashayekhi F, [Crossref], [Google Scholar], [Publisher] Safarpoor Dehkordi F, Sakhaei MH, [39] Torkan S, Shahreza MH. VacA, CagA, IceA Masoudimanesh Μ, Khameneie MK. and OipA genotype status of Helicobacter pylori Helicobacter pylori in vegetables and salads: isolated from biopsy samples from Iranian dogs. antimicrobial resistance genotyping and properties. BioMed Research International. Tropical Journal of Pharmaceutical Research. **2016** 4;15(2):377-84. [Crossref], [Google **2014** 12;2014: 757941. [Crossref], [Google Scholar], [Publisher] Scholar], [Publisher] [40] Tosan F, Rahnama N, Sakhaei D, Fathi AH, [42] Yazdanian M, Rahmani A, Tahmasebi E, Yari A. Effects of doping metal nanoparticles in Tebyanian H, Yazdanian A, Mosaddad SA. hydroxyapatite in Improving the physical and Current and Advanced Nanomaterials in chemical properties of dental implants. Dentistry as Regeneration Agents: An Update. Nanomedicine Research Medicinal Journal. Mini Reviews in Chemistry. [Google **2021**;1;6(4):327-36. [Crossref], **2021**;21(7):899-918. [Crossref], [Google Scholar], [Publisher] Scholar], [Publisher]

This journal is a double-blind peer-reviewed journal covering all areas in Chemistry, Medicinal and Petroleum. EJCMPR is published quarterly (6 issues per year) online and in print. Copyright © 2022 by ASC (<u>Amir Samimi Company</u>) which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.